Remarks

Claims 1-18, 22-25, 30-41, and 57 are pending in the application. Claims 39 and 41 have been amended. Support for the amendments can be found throughout the specification as originally filed, including the claims. Importantly, no new matter has been added. The amendments to the claims should not be construed to be an acquiescence to any of the rejections. The amendments to the claims are being made solely to expedite the prosecution of the above-identified application. The Applicants reserve the right to further prosecute the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120.

Response to Rejection Under 35 U.S.C. § 102(b)

Claims 39-41 stand rejected under 35 U.S.C. § 102(b) based on the Examiner's contention that they are anticipated by U.S. Patent No. 5,879,705 (the "'705 patent"). Applicants respectfully traverse this rejection.

Applicants submit that the '705 patent does not anticipate claims 39-41 because the '705 patent does not disclose a pharmaceutical composition consisting essentially of the components enumerated that is flowable and suitable for injection.

In order to anticipate a claim, a single source must contain all of the elements of the claim. *See Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569 (Fed. Cir. 1984).

The Examiner cites Examples 5 and 7 of Table 1 in column 7 of the '705 patent but these examples and others disclosed therein are pellets for oral administration. See column 7, lines 15-26. The pharmaceutical compositions are solid and are not flowable or suitable for injection.

Applicants disclose and claim pharmaceutical compositions consisting essentially of a non-polar biocompatible oil loaded with high amounts of a polar inorganic salt of an analgesic, with or without a minimal amount of solvent, that is still flowable and

therefore suitable for injection. Such a unique composition allows for novel treatment regimens and more sustained therapeutic effects. See page 2 of the specification.

Because the '705 patent does not disclose pharmaceutical compositions that are flowable and suitable for injection, Applicants submit that the '705 patent does not disclose each and every limitation of claims 39-41. Applicants accordingly request the withdrawal of the 35 U.S.C § 102(b) rejection of claims 39-41 over the '705 patent.

Response to Rejection Under 35 U.S.C. § 103(a)

Claims 1-18, 22-25, 30-41, and 57 stand rejected under 35 U.S.C. § 103(a) based on the Examiner's contention that they are obvious over Katzung in view of Lostritto and Remington Pharmaceutical Sciences, 18th ed., 1990, pages 294-298 and 1300-1304 ("Remington"). Applicants respectfully traverse this rejection.

A *prima facie* case of obviousness under 35 U.S.C. § 103(a) requires (1) a suggestion or motivation in the references themselves or generally known in the art, to combine the references, (2) a reasonable expectation of success to combine, and (3) a teaching, via the combination, of all the claimed limitations. Applicants submit that the combined references do not teach all of the claimed limitations because they do not teach a composition consisting essentially of a biocompatible oil and an inorganic salt of a caine analgesic agent; the references provide no motivation to prepare such a composition without solubility aids, such as surfactants; and there is no reasonable expectation that without some sort of solubilizing aid such a composition could be flowable and suitable for injection.

Katzung is relied upon by the Examiner for teaching dosages of lidocaine for parenteral use but teaches nothing about the lidocaine composition administered. There is no teaching of any formulation, never mind a biocompatible oil formulation, and never mind the absence of agents that would materially affect the basic and novel characteristics of the claimed invention. For a teaching of a lidocaine formulation, one of ordinary skill in the art has to turn to Lostritto, but Lostritto teaches away from the claimed invention.

Lostritto is relied upon by the Examiner for teaching enhancing the solubility of lidocaine in sesame oil by using water (a phosphate buffer), non-ionic surfactants

(Arlacel-20 and Brij-96), and an anionic surfactant (sodium lauryl sulfate) (see page 221, under Methods). Lostritto further teaches that "previous studies have demonstrated the need and feasibility of submicron emulsion systems as potential drug delivery systems to enhance solubility, stability, and to prolong drug delivery," and that "in the present study, 30% sesame oil in buffer submicron emulsions are prepared using a previously described nonionic surfactant mixture" (see page 220, column 1). A 30% sesame oil in buffer submicron emulsion means 70% of the formulation is water, which one of ordinary skill in the art would certainly recognize as being useful for dissolving a salt. Lostritto further teaches away from the claimed invention by stating in its conclusions that "free lidocaine in the aqueous external phase of the emulsion serves as the kinetic driving force for diffusion." See page 224, under Conclusions. Applicants submit that a fair reading of Katzung and Lostritto provides no motivation to one of ordinary skill in the art to prepare a pharmaceutical composition consisting essentially of a biocompatible oil and an inorganic salt of a caine analgesic because Lostritto teaches that solubility aids such as water, nonionic surfactants, and anionic surfactants are not only necessary for the preparation of the composition but are also the driving force behind the diffusion rates.

Applicants further submit that Remington does not cure what Katzung and Lostritto combined lack. In fact, Applicants submit that Remington strongly teaches further from the claimed invention. The sections in Remington cited by the Examiner describe coarse dispersions, emulsions, and diluting agents.

The use of surface-active agents (surfactants) is strongly recommended with coarse dispersions. Remington teaches that they "greatly facilitate wetting of lyophobic powders and assist in the removal of surface air that shearing alone may not remove; thus the clumping tendency of the particles is reduced. Moreover, lowering of the surface free energy by the adsorption of these agents directly reduces the thermodynamic driving force opposing dispersion of the particles." See the bottom of page 294.

The first line of the Emulsion section on page 298 states that "[a]n emulsion is a dispersed system containing at least two immiscible liquid phases." The present invention consists essentially of a salt of a caine analgesic and a biocompatible oil.

Even so, Remington recognizes the inherent instability of suspensions of oppositely polar substances, such as oil and a salt, and teaches that the presence of an emulsifying agent is beneficial: "[i]n addition to this flocculation effect, also observed with suspensions, the dispersed particles can coalesce, or fuse, and this can result in the eventual destruction of the emulsion. In order to minimize this effect a third component, the emulsifying agent, is added to the system to improve its stability. The choice of emulsifying agent is critical to the preparation of an emulsion possessing optimum stability." See page 298, column 1 under "Emulsions in Pharmacy" heading.

Lastly, in the section titled "Diluting Agents," Remington teaches that "[t]he best diluting agent is usually the best solvent for the drug." See page 1300, column 1. The present invention does just the opposite. It claims a composition consisting essentially of a biocompatible oil (non-polar) and an inorganic salt of a caine analgesic (polar). It can not be said that a non-polar oil is the best solvent for a polar salt.

Applicants submit that a fair reading of Katzung in view of Lostritto and Remington teaches one of ordinary skill in the art that a pharmaceutical composition of an inorganic salt should contain a solvent that the salt is soluble in, and if it doesn't then solubility aids such as surfactant agents should be used. Neither teaching provides motivation or the likely chance of success of the claimed invention which consists essentially of a biocompatible oil and inorganic salt of a caine analgesic.

Applicants have surprisingly found that such a formulation can not only be prepared but is suitable for administration by injection and gives an improved release rate of the caine analgesic.

Fees

The Applicants believe they have provided for the required fees in connection with the filing of this paper. Nevertheless, the Director is hereby authorized to charge any additional required fee to our Deposit Account, **06-1448**.

Conclusion

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the pending claims are now in condition for allowance and early notification to this effect is earnestly solicited. If any questions are raised by this Amendment and Response, the Examiner is urged to contact the undersigned at the telephone number listed below.

Respectfully submitted,
Patent Group
Foley Hoag LLP

By: Michael J. DiVerdi

Michael J. DiVerdi
Reg. No. 51,620
Agent for Applicants

155 Seaport Boulevard
Boston, MA 02210
Telephone: (617) 832-1000
Telecopier: (617) 832-7000

Date: 2/20/07